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A PROSPECTIVE OBSERVATIONAL STUDY ON THE EFFICACY OF PANTOPRAZOLE-DOMPERIDONE COMPARED WITH PANTOPRAZOLE-ITOPRIDE COMBINATION IN TYPE 2 DIABETIC GASTROPARESIS – A PILOT STUDY

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ABSTRACT

Background: Diabetic Gastroparesis is outlined as a clinical condition that is characterized by upper GI dyspeptic symptoms (nausea, bloating, vomiting, weight loss, post prandial fullness) in association with delayed gastric emptying leading to poor glycemic management, poor nutrition and dehydration. We intend to assess which of the combination is better when comparing Pantoprazole-Itopride with Pantoprazole-Domperidone. **Methods**: A prospective observational study with total of 20 diabetic patients who visited the Department of Gastroenterology at a tertiary care hospital and with abdominal symptoms as their chief complaints were enrolled for the study in whom blood glucose tests were performed, which revealed Diabetic Gastroparesis condition. **Results**: A Total of 20 patients with Diabetic Gastroparesis fulfilling the study criteria were included. Using paired t-test, statistical analysis clearly depicts that Pantoprazole – Itopride with a p value 0.001 is comparatively effective than Pantoprazole – Domperidone with a p value of 0.03. **Conclusion**: The aim of the study was to promote the symptomatic betterment in Diabetic Gastroparesis patients thereby to improve the quality of life in them. The present study demonstrated that the symptoms presented by the patient was improved after receiving the therapy and was recorded higher in Pantoprazole – Itopride group when compared to Pantoprazole – Domperidone group. However larger number of samples and longer duration of study are required to produce valuable and reliable results.

KEYWORDS: Diabetic Gastroparesis, symptomatic betterment, adherence, gastric emptying, quality of life, efficacy, blood glucose.

INTRODUCTION

Diabetic Gastroparesis is outlined as a clinical condition that is characterized by upper GI dyspeptic symptoms (nausea, bloating, vomiting, weight loss, post prandial fullness) in association with delayed gastric emptying leading to poor glycemic management, poor nutrition and dehydration.[1,2] Usual treatment for Diabetic Gastroparesis includes nutritional assessment, Dietary modification, Glycemic management, Prokinetic agents and Proton pump inhibitors.[3,4,5]

The present study was carried out to assess which combination therapy is better, combination of Pantoprazole – Domperidone or Pantoprazole - Itopride in the treatment of Diabetic Gastroparesis and to analyze which combination have better adherence.

MATERIALS AND METHODS

In this study, a total of 20 patients who visited the Department of Gastroenterology at a tertiary care hospital who were diabetic and with abdominal symptoms as their chief complaints were enrolled for the study in whom blood glucose tests were performed, which reveals Diabetic Gastroparesis condition. Physical examinations, Small Intestine Bacterial Overgrowth (SIBO) tests and Thyroid Stimulating Hormone (TSH) levels were also assessed and those presented with Diabetic Gastroparesis symptoms were recruited for the study.

Inclusion Criteria

- 40-70 yrs. of age group
- Patients diagnosed as Diabetic Gastroparesis.
- Patients who give informed consent.

Exclusion Criteria

- Patients with
  - Other Endocrine disorders such as Hypothyroidism (as hypothyroidism is another reason for Gastroparesis)
  - With motor neuron disorders
  - Who are taking other Proton Pump Inhibitors (PPI's) and Prokinetic drugs
  - Eating disorders (Bulimia nervosa)
  - Drug induced gastroparesis such as Tricyclic antidepressants, Calcium channel blockers etc.
- Pregnant and Lactating women.

Total of 20 patients were divided into 2 groups, each group containing 10 patients. For treating Diabetic Gastroparesis, a combination of Pantoprazole 40mg – Itopride 150mg (Pantop - IT) capsules for a period of 14 days was administered by Group I.

A combination of Pantoprazole 40 mg – Domperidone 30mg (Pantop - DSR) capsules for a period of 14 days was administered by Group II. At the beginning of the study informed consent were obtained from the patients.

The symptomatic betterment was assessed using Gastroparesis Cardinal Symptom Index (GCSI) Scale. The scale was given twice to the patients. First the scale was given before administering drug and after completing the 14 days therapy, the patients were instructed to fill the scale for the second time and the scores were assessed before and after therapy. Medication Adherence was assessed using Adherence to Refill Medications Scale (ARMS). The questionnaire was given to the patient after the therapy. Nutritional status was also assessed using Mini Nutritional Assessment (MNA) Scale which was given to the patient before and after initiating the therapy.

Statistical Analysis

Data were presented as mean SE±. Differences between continuous variables were analyzed by using paired t test. In all test, a p value of <0.05 was considered to be significant.

RESULT

In this study, a total of 20 patients were taken and divided into 2 groups, containing 10 patients in each group. First group is treated with Pantop IT capsules and Pantop DSR capsules for the second group. No patients were excluded during the study period as per the exclusion criteria. No patients had taken the combination drugs before entering into the study. None of them had taken Proton Pump Inhibitors (PPI's), Prokinetic drugs, tricyclic antidepressants or calcium channel blockers within one month prior to the study.

1. Age Wise Distribution

Among 20 patients screened, the age distribution data shows 40% of patients were in the age group of 50-60 years, 45% of patients were in the age group of 60-70 years and 15% of patients were in the group of 70-80 years.

Table 1: Percentage distribution of age in patients participating in the study.

Age in years	No of patients (N)	Percentage
50 - 60	8	40%
60 - 70	9	45%
70 - 80	3	15%

2. Gender Wise Distribution

Gender wise distribution data of overall study population is given in (Table 2) and it shows 50% of male patients and 50% of female patients were participated in the study.

Table 2: Percentage gender distribution in patients participating in the study.

Gender	P-IT		P-DSR		Total	
	No. of Patients	Percentage (%)	No. of Patients	Percentage (%)	No. of Patients	Percentage (%)
Female	5	50	5	50	10	50
Male	5	50	5	50	10	50
Total	10	100	10	100	20	100

3. Assessment of Symptomatic Betterment

Gastroparesis Cardinal Symptom Index (GCSI) is a reliable and valid instrument for measuring the symptom severity in patients with Gastroparesis. It is a 9-item questionnaire where the patient is asked to encircle the symptoms experienced by them. If the patient has not experienced a particular symptom 0 is encircled. If the symptom has been very mild, 1 is encircled. If the symptom has been mild, 2 is encircled. If it has been moderate, 3 is encircled. If it has been severe, 4 and for very severe, 5 is encircled respectively and the sum of their values are taken as total score.[6]

Table 3: Percentage of symptoms present in both groups.

SYMPTOMS	P-IT		P-DO		Total	
	N	%	N	%	N	%
Abdominal pain	9	90	7	70	16	80
Regurgitation	6	60	9	90	15	75
Loss of appetite	6	60	8	80	14	70
Flatulence	4	40	8	80	12	60
Post prandial fullness	6	60	6	60	12	60
Bloating	10	100	10	100	20	100

Table 3 represents the percentage of symptoms in both group I and group II where 100 % of the patients in both groups shows bloating and 80% of them shows abdominal pain whereas regurgitation was seen in 75% of patients.

3.1. Assessment of symptomatic betterment before and after therapy in Group 1 patients.

Table 4: Mean symptom score of patients before & after therapy in Group I patients.

Group	N (No of subjects)	Gastroparesis Cardinal Symptom Index (GCSI)		Mean
P-IT	10	Before Therapy	168	16.8
	10	After Therapy	101	10.1

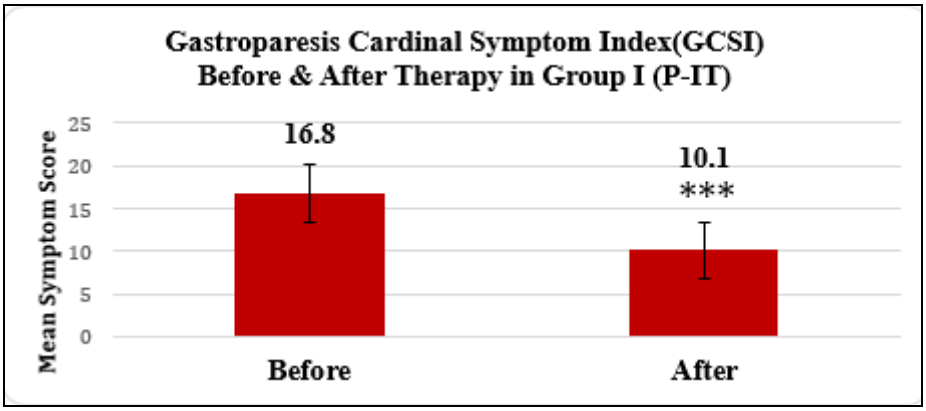

Figure 1: Comparison of symptomatic assessment before and after therapy in Group I.

****** - p≤0.001***

- Abdominal pain :: ***
- Regurgitation :: ***
- Loss of appetite:: ***
- Flatulence :: ***
- Post Prandial Fullness :: ***
- Bloating :: ***

The result shows, there is a significant symptomatic improvement in group 1 patients after receiving Pantoprazole-Itopride combination.

A study by Abid Shah et al. demonstrated that addition of Itopride before meals facilitates food delivery to the intestine, increases incretin secretion, and thus improves the glycaemic parameters implying the beneficial effects of Itopride in glycaemic management.[7]

3.2. Assessment of symptomatic betterment before and after therapy in Group II patients

Table 5: Mean symptom score of patients before & after therapy in Group II patients.

Group	N (No of subjects)	Gastroparesis Cardinal Symptom Index (GCSI)		Mean
P-DSR	10	Before Therapy	176	17.6
	10	After Therapy	143	14.3

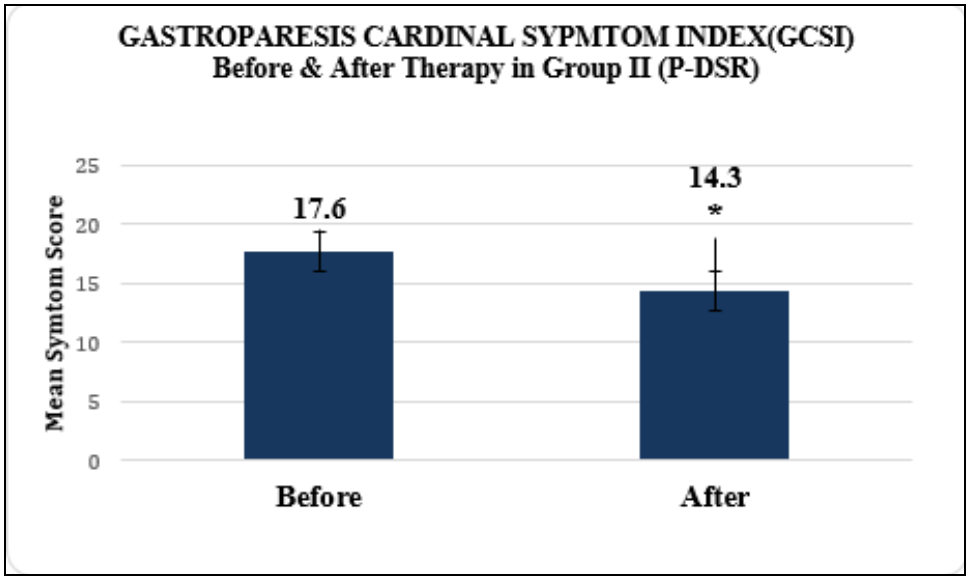

Figure 2: Comparison of symptomatic assessment before and after therapy in Group II.

**** - p≤0.05***

- *Abdominal pain :: **
- *Regurgitation :: **
- *Loss of appetite :: **
- *Flatulence :: **
- *Post Prandial Fullness :: **
- *Bloating :: **

From the above table and graph, the patients in group II showed symptomatic improvement after receiving Pantoprazole-Domperidone.

Domperidone which is a dopamine-2 receptor antagonist effective in reducing symptoms of nausea and vomiting in patients with Diabetic Gastroparesis and does not cross the blood brain barrier and is associated with fewer Central Nervous System (CNS) effects.[8]

3.3. Comparison of Symptomatic Assessment Before and After Therapy in Group I & Group II

Table 6: Mean symptom score of patients before & after therapy in Group I & Group II.

Group	(N) No of subjects	Gastroparesis Cardinal Symptom Index (GCSI) Mean Score	
		Before Therapy	After Therapy
P - IT	10	16.8	10.1
P-DSR	10	17.6	14.3

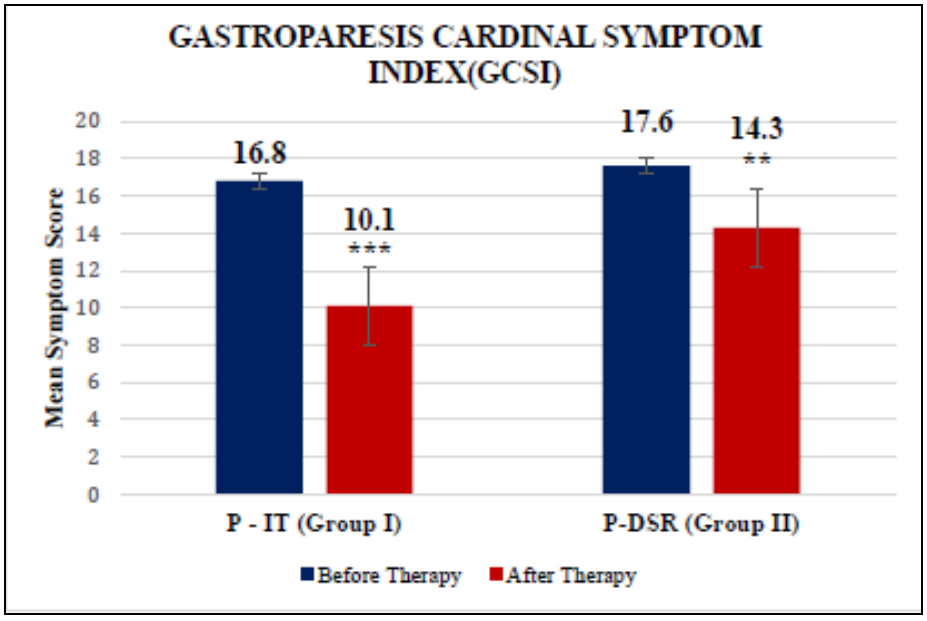

Figure 3: Comparison of symptomatic assessment before & after therapy in Group I & Group II.

****** - p≤ 0.001, ** - p - 0.01***

By comparing the before and after therapy in both groups, it can be concluded that the symptomatic betterment was greater in patients receiving Pantoprazole–Itopride when compared to patients receiving Pantoprazole-Domperidone.

Pantoprazole – Itopride therapy efficiently improve the symptoms such as abdominal pain, regurgitation, loss of appetite, flatulence, post prandial fullness and bloating than Pantoprazole-Domperidone.

A study of Kumar et. Al,[9] where minority of the patients had symptoms of Gastro Oesophageal Reflux Disease (GERD) were present without any endoscopically visible mucosal injury. At the end of the follow up, relief of symptoms was more with a combination of Itopride and Rabeprazole in comparison to the combination of Domperidone and Rabeprazole implying that the Itopride – Rabeprazole combination is symptomatically better than Domperidone and Rabeprazole.

4. Assessment of Medication Adherence

Medication Adherence is measured by Adherence to Refill Medication Scale (ARMS), a 12-item questionnaire which should be reverse coded. Then added up the points.

The range of possible scores is 12 to 48. Lower scores indicate better adherence. Scores can be treated as a continuous measure or dichotomized as 12 or >12.

The Adherence to Refill Medication Scale (ARMS) is a valid and reliable medication adherence scale with good performance characteristics even among low-literacy patients and it correlated significantly with the Morisky adherence scale and it correlated more strongly with measures of refill adherence than did the Morisky scale.[10]

Table 7: Medication Adherence assessment in Group I and Group II.

Group	(N) No of Subjects	Adherence to Refill Medication Scales (ARMS)	
		Mean	sd
P-IT	10	11.7	2.221
P-DSR	10	11.6	2.15

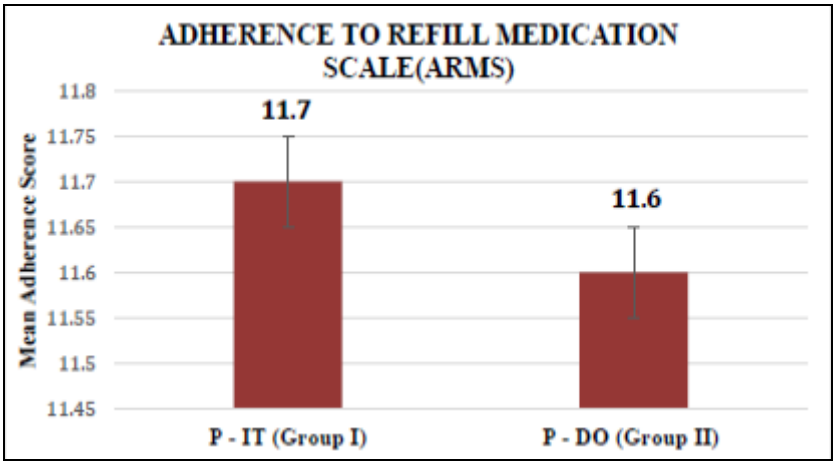

Figure 4: Medication Adherence assessment in Group I and Group II after therapy.

However as there is no statistically significant difference ($p > 0.05$), it can be concluded that the medication adherence was almost equivalent in Group I and Group II.

5. Assessment of Nutritional Status

Nutritional Assessment is done by Mini Nutritional Assessment (MNA) scale which is a 6-item scale where the maximum points are 14.

Scoring as follows: -

- 12-14 points: Normal nutritional status
- 8-11 points: At risk of malnutrition
- 0-7 points: Malnourished.

5.1 Comparison of Nutritional Status in Group I & Group II Before Therapy

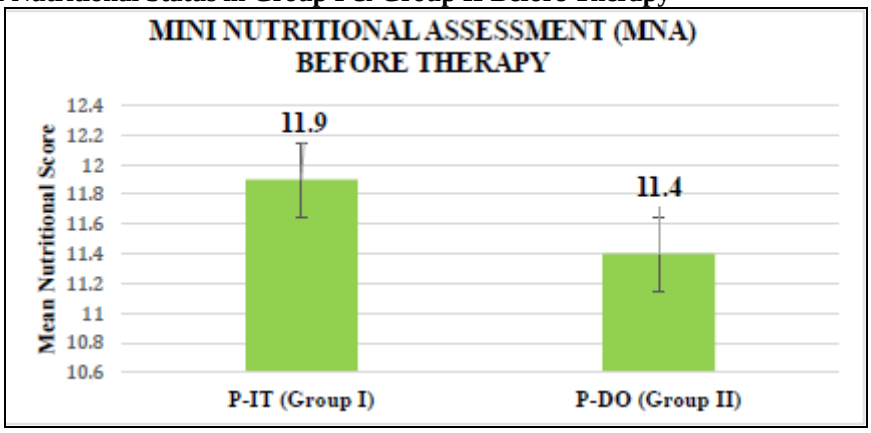

Figure 5: Comparison of Nutritional Status in Group I & Group II Before Therapy

There is no statistically significant difference in both the groups, hence it is assumed that the nutritional status is equivalent in both the groups.

5.1 Comparison of Nutritional Status in Group I & Group II After Therapy

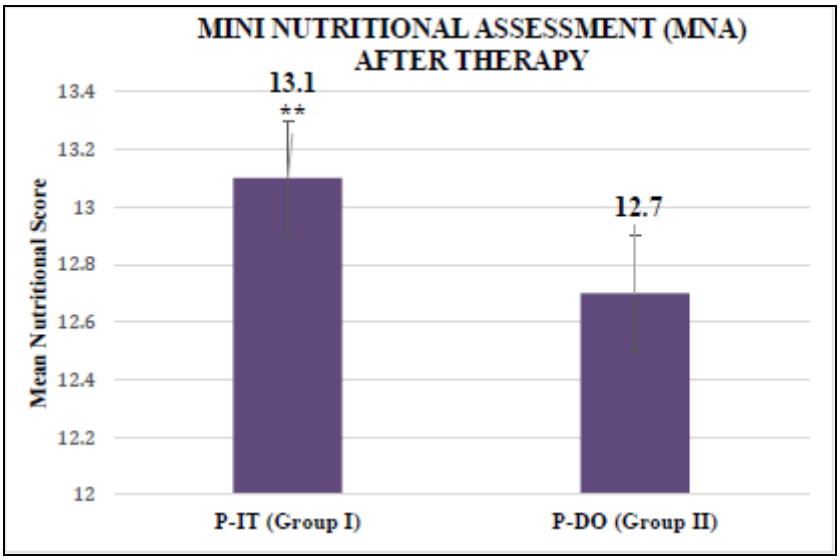

Figure 6: Comparison of Nutritional Status in Group I & Group II After Therapy

***** - p ≤0.01***

From the above graph it is assessed that the Group I receive Pantoprazole-Itopride showed improvement in the nutritional status.

5.3 Comparison of Nutritional Status Before and After Therapy in Group I & Group II.

Table 8: Comparison of nutritional status before and after therapy in Group I & Group II.

Group	(N) No of subjects	Mini Nutritional Assessment (MNA) Mean Score	
		Before Therapy	After Therapy
P - IT	10	11.9	13.1
P-DSR	10	11.4	12.7

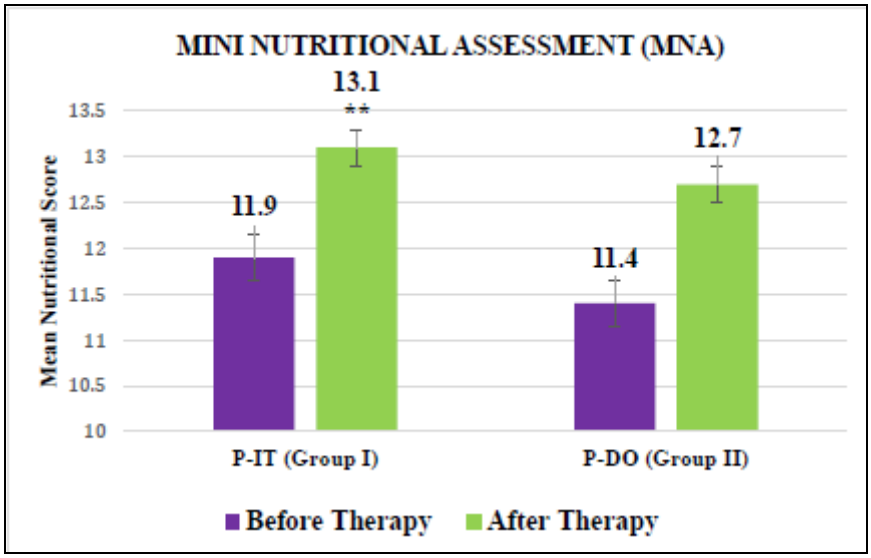

Figure 7: Comparison of nutritional status before and after therapy in Group I & Group II.
- $p \leq 0.01$

By comparing the nutritional status before and after therapy in both groups, it can be concluded that the nutritional status was better in patients receiving Pantoprazole–Itopride when compared to patients receiving Pantoprazole-Domperidone, where both the groups receiving specific patient counselling on diet plan.

Patients with Gastroparesis have symptoms associated with eating, resulting in food aversion and inadequate oral intake and may experience protracted nausea and vomiting, making it difficult to maintain hydration and nutrition. Thus, patients with Gastroparesis are at risk for weight loss, malnutrition, vitamin and mineral deficiencies.[11]

Although there is no accurate evidence to support the nutritional status improvement with any of the drug therapy in our study, Pantoprazole – Itopride group could sufficiently improve the symptoms which hinders the nutritional adequacy as depicted in the above graph.

DISCUSSION

In our study we assessed the symptomatic betterment before and after therapy and medication adherence of Diabetic Gastroparesis patients. Prior to the therapy, most of the subjects showed significant gastrointestinal symptoms, but after the therapy most of these subject's symptoms were decreased which implies that the subjects experienced symptomatic betterment from both the therapy.

In this study, two groups comprised of 10 subjects each and group I administered with Pantoprazole 40 mg – Itopride 150mg (Pantop-IT capsules) and group II with Pantoprazole 40mg – Domperidone 30mg (Pantop-DSR capsules).

The studies by Kamel.[12] and Malhotra et. al[13] showed symptomatic betterment in patients receiving the combination of Pantoprazole and Itopride. Similarly, in Ndraha et. al[14] study shows that, the combination of PPIs with prokinetics improved the effect of PPIs and in our study, we have shown similar results that Pantoprazole – Itopride combination is effective than Pantoprazole –Domperidone combination.

In the study of Singhal and Shipra [15] the drug combination of Pantoprazole and Domperidone achieved high endoscopic oesophageal healing rates and our study also shows similar result when compared to this study.

In a clinical comparative evaluation of the efficacy and tolerability of Itopride and Domperidone in patients with Non-ulcer Dyspepsia (NUD) by Prabha et. al. [16], moderate to complete symptomatic relief was observed in 22 patients in the Itopride group and 19 patients in the Domperidone group which implies that Itopride is more efficient compared to Domperidone in relieving the symptoms of NUD and our study also shown similar result carried out in 20 patients giving Itopride in 10 people and Domperidone in another 10 people shows that Itopride is more effective when compared to Domperidone.

In a study showing efficacy and tolerability of Rabeprazole and Domperidone in the treatment of patients suffering from Gastro-Esophageal Reflux Disease (GERD) by Shahani and Savita, [17] it is evident that the Rabeprazole and Domperidone provided desired relief of symptoms of Gastro-Esophageal Reflux Disease(GERD) stating they are significantly efficacious and well tolerated, also improving the quality of life of patients suffering from Gastro Esophageal Reflux Disease(GERD).Similarly, in our study also less significant betterment was shown in patients given with Pantoprazole- Domperidone compared to Pantoprazole –

Itopride which is highly significant and also improved quality of life of patients.

Studies by Heckert and Parkman,[18] shows that early satiety, postprandial fullness, and overall symptom severity significantly improved from baseline to the final week of treatment, whereas nausea had borderline improvement. Domperidone improves symptoms of Gastroparesis, reducing overall Gastroparesis symptom severity and decreasing early satiety, postprandial fullness, and nausea but in our study Domperidone shows less symptomatic improvement when compared to Itopride which shown greater improvement.

In the study by Pradeep et al. the symptomatic relief was significantly more in Pantoprazole plus Itopride group than Pantoprazole alone after 4 weeks of therapy and that addition of a Prokinetic agent like Itopride along with Proton Pumb Inhibitor (PPI) like Pantoprazole, results in complete resolution of dyspeptic symptoms and improvement in the quality of life,[19] and this shows a result similar to our study result.

Another similar study by Pradeep et.al,[20] has shown that addition of Prokinetic agent along with Proton Pump Inhibitor (PPIs) has better tolerability compared to Proton Pump Inhibitor (PPIs) monotherapy.

A study by Kim et al[21] showed that Itopride 100 mg three times a day improved Gastro-Esophageal Reflux Disease (GERD) symptoms and decreased oesophageal acid exposure and when compared, a similar result with significant improvement was shown in our study who are treated with Itopride.

Even though there wasn't any statistically significant difference in the medication adherence score which was assessed using Adherence to Refill Medication Scales (ARMS), group I receive Pantoprazole – Itopride showed better tolerance than group II receiving Pantoprazole – Domperidone.

Using Mini Nutritional Assessment (MNA) scale, the nutritional status were assessed and came to a conclusion that the nutritional status of Group I (P-IT) shows higher than Group II (P-DSR) patients as it reduces the symptoms related to Gastroparesis which causes delay in food absorption. Patient counselling was given on diet plan for those who are at risk of nutritional deficiency.

As these symptoms influences the daily activities, physical health and psychological state of a person, it was mandatory to provide symptomatic betterment in patient's in order to improve the quality of life in them.
Thus, from the study it can be concluded that the symptomatic betterment were higher in group I receiving Pantoprazole – Itopride compared to group II receiving Pantoprazole – Domperidone.

CONCLUSION

The aim of the study was to promote the symptomatic betterment thereby improving the quality of life in patients.

The present study demonstrated that the gastrointestinal symptoms presented by the patients were improved after receiving the therapy and was recorded higher in Pantoprazole – Itopride group.

The symptoms of the subjects from both the group are similar before the therapy but after the therapy it was found that the patients receiving Pantoprazole – Itopride showed significant betterment in symptoms compared to the second group Pantoprazole – Domperidone for the short term therapy of 14 days which was assessed using the Gastro Cardinal Symptom Index (GCSI).

However larger number of samples and longer duration of study are required to produce valuable and reliable results. As a shortcoming, the study could not assess any significant results in the Medication adherence due to the shorter study duration.

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